Final report-Teratologic Evaluation of FDA 71-16 (**Guar Gum**) in Mice, Rats, Hamsters & Rabbits 8/25/72

#24

FOOD AND DRUG LABORATORIES, INC.

MAURICE AVENUE AT 58TH STREET, MASPETH, NEW YORK 11378

FINAL

August 25, 1972

Teratologic Evaluation of FDA 71-16 (Guar Gum) in Mice, Rats, Hamsters and Rabbits

M I C E

Food and Drug Research Laboratories
INCORPORATED

Maurice Avenue at 58th Street
Maspeth, New York 11378
Telephone: TWining 4-0800
Cable: Foodlabs, New York

FINAL REPORT

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date August 25, 1972

Laboratory No. 0893 f
Contract No. FDA 71-260

Sample: Fine tan powdered material

Marking: FDA 71-16 (Guar Gum)

Examination Requested: Teratologic evaluation of FDA 71-16 in mice.

Procedure: See Appendix I

Results: See Tables 1 through 4 and Appendix II

Conclusion: Subject to reexamination in the light of later findings, the following is concluded:

"The administration of up to 170 mg/kg (body weight) of the test material to pregnant mice for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

In a concurrent group of mice dosed at a level of 800 mg/kg, however, a significant number of maternal deaths occurred (6 out of 29). The surviving dams appeared completely normal and bore normal fetuses with no effect on the rate of nidation or survival of live pups in utero. It was concluded that the test material was not a teratogen to mice under the conditions of the test."

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge

Kenneth Morgareidge, Ph.D.
Vice President

Comment: Attention is called to the fact that this is the ninth of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 36 compounds will have been tested in 18 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 81 through 86

Material: FDA 71-16

Table 1

Fate Summary
(Mice)

Date July 17, 1972

Laboratory No. 0893 f

Group	Material	Dose mg/kg	Total		At Term	
			Mated	Pregnant	Surviving (Total)	Number Pregnant
81	Sham	0	24	19	23	19
82	Aspirin	150	27	21	25	19
83	FDA 71-16	8	22	18	22	18
84	FDA 71-16	37	26	21	26	21
85	FDA 71-16	170	25	20	24	20
86	FDA 71-16	800	29	19	23	14

* Positive Control

** Administered as a suspension in anhydrous corn oil; 1 ml per kg of body weight

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group: 81 through 86 Date: July 17, 1972

Material: FDA 71-16 Laboratory No.: 0893 f

Table 2
Reproduction Data
(Mice)

Group:	81	82	83	84	85	86
Dose (mg/kg):	Sham	Aspirin**	8	37	170	800
Pregnancies						
Total No.	19	21	18	21	20	19
Died or Aborted (before Day 17)	1	2	0	0	1	6
To term (on Day 17)	19	19	18	21	20	14
Corpora Lutea						
Total No.						
Average/dam mated						
Live Litters						
Total No.*	19	19	18	21	20	11
Implant Sites						
Total No.	223	225	218	260	230	153
Average/dam*	11.7	11.8	12.1	12.4	11.5	10.9
Resorptions						
Total No.*	8	17	10	10	16	28
Dams with 1 or more sites resorbed	6	9	7	5	10	6
Dams with all sites resorbed	0	0	0	0	0	2
Per cent partial resorptions	31.6	47.4	38.9	23.8	50.0	42.9
Per cent complete resorptions	--	--	--	--	--	14.3
Live Fetuses						
Total No.	212	205	203	246	212	123
Average/dam*	11.2	10.8	11.3	11.7	10.6	8.79
Sex ratio (M/F)	0.75	0.71	0.65	0.61	0.85	0.76
Dead Fetuses						
Total No.*	3	3	5	4	2	2
Dams with 1 or more dead	3	3	4	4	2	1
Dams with all dead	0	0	0	0	0	0
Per cent partial dead	15.8	15.8	22.2	19.0	10.0	7.14
Per cent all dead	--	--	--	--	--	--
Average Fetus Weight, g	0.90	0.85	0.86	0.89	0.83	0.78

*Includes only those dams examined at term.
**Positive Control - 150 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 | Table 3 | Laboratory No. 0893 f

Material FDA 71-16 | Date July 17, 1972

Summary of Skeletal Findings (Mice)

Findings	Group No.	81	82	83	84	85	86
	Dose (mg/kg)	Sham	Aspirin**	8	37	170	800
Live Fetuses Examined (at term)		144/18 (a)	146/19	141/18	148/21	148/20	85/11
Sternebrae							
Incomplete oss.		55/13	61/16	69/17	122/20	77/15	44/10
Scrambled							
Bipartite		6/4		2/2	21/11	13/9	4/4
Fused							
Extra			1/1		1/1	2/2	2/2
Missing		22/10	41/9	23/8	25/7	14/8	31/8
Other							
Ribs							
Incomplete oss.							
Fused/split							
Wavy							
Less than 12							
More than 13		7/5	8/4	11/8	9/7	7/4	14/5
Other							
Vertebrae							
Incomplete oss.			4/2	4/2	2/2		
Scrambled							
Fused							
Extra ctrs. oss.						1/1	
Scoliosis							1/1
Tail defects							
Other							
Skull							
Incomplete closure		2/2		1/1	4/1		
Missing							
Craniostosis							
Other							
Extremities							
Incomplete oss.		1/1		7/2	4/3		
Missing							
Extra							
Miscellaneous							
Hyoid; missing		31/14	50/12	58/13	43/17	34/13	42/10
Hyoid; reduced		24/11	19/11	28/12	41/16	24/11	3/3
Pelvic girdle; missing					2/1		

* Numerator=Number of fetuses affected; Denominator=Number of litters affected
** Positive control at 150 mg/kg
a) One litter lost

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 Date July 17, 1972

Material FDA 71-16 Laboratory No. 0893 f

Table 3-a

Summary of Soft Tissue Abnormalities
(Mice)

Group	Material	Dose level mg/kg	Dam	Pup	Description
None Observed					

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86

Species Mice

Table 4

Average Body Weights*

Date July 17, 1972

Laboratory No. 0893 f

Group	Material	Dose Level	Day 0	6	11	15	17**
		mg/kg	g				
81	Sham	0.0	29.4	31.3	34.0	42.4	47.6 (19)
82	Aspirin***	150.0	29.1	32.8	33.8	41.2	46.2 (19)
83	FDA 71-16	8.0	27.6	30.9	32.5	38.2	44.8 (18)
84	FDA 71-16	37.0	29.0	31.9	33.9	42.0	48.7 (21)
85	FDA 71-16	170.0	29.0	31.8	32.9	39.8	44.9 (20)
86	FDA 71-16	800.0	28.6	30.9	29.5	35.1	40.2 (14)

* Of pregnant dams
** Number of surviving dams in parentheses (c.f. Table 1)
*** Positive control

Appendix I

Teratology Study in Mice

Virgin adult female albino CD-1 outbred mice were individually housed in disposable plastic cages in temperature and humidity-controlled quarters with free access to food and fresh tap water. They were mated with young adult males, and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubation; the controls were sham treated.

Body weights were recorded on Days 0, 6, 11, 15, and 17 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities which may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 17 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam was examined in detail for anatomical normality.

All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing 10X magnification. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 81 | Appendix II | Date July 17, 1972

Material Sham | Reproduction Data in Mice (Individual) | Laboratory No. 0893

Dose 0.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
S 3241	P		13	13		6	7		1.05	
S 3242	P		11	11		6	5		0.98	
S 3243	NP		0						----	Died Day 10
S 3244	P		18	17		7	10	1	0.97	
S 3245	P		12	11		4	6	1	1.02	
S 3246	P		11	9		3	6	2	1.04	
S 3247	P		17	17		7	10		1.11	
S 3248	P		13	13		6	7		0.85	
S 3249	P		10	10		5	5		0.84	
S 3250	NP		0						----	
S 3251	P		13	12	1	6	6		0.78	
S 3252	P		11	10	1	3	7		0.86	
S 3253	NP		0						----	
S 3254	NP		0						----	
S 3255	P		8	8		--	--		0.90	
S 3256	P		10	10		4	6		0.83	
S 3257	P		11	10	1	5	5		0.85	
S 3258	P		11	9		3	6	2	0.74	
S 3259	NP		0						----	
S 3260	P		11	11		5	6		0.77	
S 3261	P		14	14		5	9		0.94	
S 3262	P		6	6		3	3		0.89	
S 3263	P		13	12		4	8	1	0.82	
S 3264	P		10	9		4	5	1	0.80	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 82 | Appendix II | Date July 17, 1972

Material Aspirin | Reproduction Data in Mice (Individual) | Laboratory No. 0893

Dose 150.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
A 3241	P		11	11		--	--		----	Died Day 9
A 3242	P		14	13		5	8	1	0.95	
A 3243	P		14	13		4	9	1	0.74	
A 3244	P		11	11		4	7		0.96	
A 3245	P		11	11		4	7		1.06	
A 3246	P		14	14		6	8		0.91	
A 3247	P		11	9		4	5	2	0.88	
A 3248	P		11	10		7	3	1	0.93	
A 3249	NP		0						----	
A 3250	P		11	11		4	7		0.97	
A 3251	P		9	8	1	4	5		1.14	
A 3252	P		12	11	1	7	4		1.09	
A 3253	P		13	13		4	9		0.62	
A 3254	P		16	10		4	6	6	0.71	
A 3255	P		12	11		4	7	1	0.64	
A 3256	P		13	13		3	10		0.83	
A 3257	NP		0						----	
A 3258	NP		0						----	
A 3259	P		10	9		3	6	1	0.86	
A 3260	NP		0						----	
A 3261	NP		0						----	
A 3262	NP		0						----	
A 3263	P		11	10		6	4	1	0.64	
A 3264	P		8	8		--	--		----	Died Day 11
A 3265	P		10	9	1	6	3		0.70	
A 3266	P		11	8		3	5	3	0.74	
A 3267	P		11	11		4	7		0.84	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEA) LABORATORIES, INC.

Group 83 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Mice (Individual) | Laboratory No. 0893 f

Dose 8.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 3001	P		14	13		5	8	1	0.91	
F 3002	P		14	14		7	7		0.85	
F 3003	P		15	14	1	5	10		0.90	
F 3004	P		14	13		8	5	1	0.93	
F 3005	P		14	12		5	7	2	0.92	
F 3006	P		12	12		4	8		0.94	
F 3007	P		13	13		5	8		0.87	
F 3008	P		10	10		3	7		0.86	
F 3009										Not assigned
F 3010	P		11	11		3	8		0.86	
F 3011	P		12	11	1	5	6		0.76	
F 3012	P		12	12		2	10		0.85	
F 3013	NP		0						----	
F 3014	P		11	9	1	3	6	1	0.78	
F 3015	P		11	9	2	5	5		0.73	
F 3016	NP		0						----	
F 3017	P		4	3		1	2	1	0.91	
F 3018	NP		0						----	
F 3019	NP		0						----	
F 3020	P		13	13		7	6		1.01	
F 3021	P		12	12		5	7		0.99	
F 3022	P		12	11		4	7	1	0.79	
F 3023	P		14	11		4	7	3	0.61	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 84

Material FDA 71-16

Dose 37.0 mg/kg

Appendix II

Reproduction Data in Mice (Individual)

Date July 17, 1972

Laboratory No. 0893 f

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 3031	P		15	15		7	8		1.02	
F 3032	P		12	12		5	7		0.95	
F 3033	NP		0						----	
F 3034	P		13	13		6	7		1.10	
F 3035	P		10	10		4	6		1.05	
F 3036	P		10	10		8	2		0.97	
F 3037	P		14	14		7	7		0.99	
F 3038	P		15	15		5	10		0.94	
F 3039	P		14	14		0	14		0.69	
F 3040	NP		0						----	
F 3041	NP		0						----	
F 3042	P		11	11		4	7		0.78	
F 3043	P		6	6		1	5		0.97	
F 3044	P		11	11		4	7		0.83	
F 3045	P		11	11		4	7		0.74	
F 3046	P		15	14		4	10	1	0.88	
F 3047	P		14	13	1	3	11		0.89	
F 3048	P		12	10		3	7	2	0.87	
F 3049	P		12	11	1	4	8		1.00	
F 3050	P		12	11	1	4	8		0.72	
F 3051	P		14	12	1	6	6	1	0.72	
F 3052	NP		0						----	
F 3053	NP		0						----	
F 3054	P		11	10		6	4	1	1.18	
F 3055	P		13	8		4	4	5	0.66	
F 3056	P		15	15		8	7		0.80	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 85

Appendix II

Date July 17, 1972

Material FDA 71-16

Reproduction Data in Mice (Individual)

Laboratory No. 0893 f

Dose 170.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 3061	P		14	14		5	9		0.96	
F 3062	P		14	13		5	8	1	1.07	
F 3063	P		13	12		4	8	1	0.87	
F 3064	P		14	14		6	8		0.87	
F 3065	P		12	11		4	7	1	0.26	
F 3066	P		14	12	1	8	4	1	0.74	
F 3067	NP		0						----	
F 3068	P		11	10		7	3	1	0.86	
F 3069	P		5	2		1	1	3	1.77	
F 3070	P		9	8		6	2	1	1.28	
F 3071	P		7	7		5	2		1.34	
F 3072	NP		0						----	
F 3073	P		13	13		4	9		0.78	
F 3074	NP		0						----	
F 3075	P		8	7	1	4	3		0.88	
F 3076	NP		0						----	Died Day 9
F 3077	P		14	14		7	7		0.65	
F 3078	P		13	13		4	9		0.80	
F 3079	P		11	10		5	5	1	0.91	
F 3080	NP		0						----	
F 3081	P		13	13		5	8		0.75	
F 3082	P		11	11		5	5		0.84	
F 3083	P		8	5		1	4	3	0.78	
F 3084	P		13	13		7	6		0.69	
F 3085	P		13	10		4	6	3	----a	

* P = Pregnant; NP = Not Pregnant

a Weight not recorded

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 86

Appendix II

Date July 17, 1972

Material FDA 71-16

Reproduction Data in Mice (Individual)

Laboratory No. 0893 f

Dose 800.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 3091	P		13	13		5	8		0.88	
F 3092	P		14	13		5	8	1	0.83	
F 3093	P		16	16		--	--		----	Died Day 8
F 3094	P		13	13		7	6		1.00	
F 3095	P		14	12		6	6	2	0.84	
F 3096	NP		0						----	
F 3097	P		11	11		6	5		0.72	
F 3098	P		9	0		--	--	9	----	
F 3099	NP		0						----	
F 3100	P		12	12		--	--		----	Died Day 7
F 3101	NP		0						----	
F 3102	P		6	0		--	--	6	----	
F 3103	NP		0						----	
F 3104	NP		0						----	
F 3105	P		12	12		5	7		0.76	
F 3106	P		10	10		3	7		0.74	
F 3107	P		11	11		4	7		0.77	
F 3108	P		14	14		--	--		----	Died Day 11
F 3109	NP		0						----	Died Day 16
F 3110	P		8	0		--	--	8	----	Died Day 9
F 3111	P		10	10		5	5		0.67	
F 3112	NP		0						----	
F 3113	NP		0						----	
F 3114	P		11	11		4	7		0.59	
F 3115	NP		0						----	
F 3116	P		8	0	2	--	--	6	0.42	
F 3117	P		11	0		--	--	11	----	Died Day 10
F 3118	NP		0						----	
F 3119	P		11	7		3	4	4	0.73	

* P = Pregnant; NP = Not Pregnant

R A T S

Food and Drug Research Laboratories
INCORPORATED

Maurice Avenue at 58th Street
Maspeth, New York 11378
Telephone: TWining 4-0800
Cable: Foodlabs, New York

FINAL REPORT

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date August 25, 1972

Laboratory No. 0894 f
Contract No. FDA 71-260

Sample: Fine tan powdered material

Marking: FDA 71-16 (Guar Gum)

Examination Requested: Teratologic evaluation of FDA 71-16 in rats

Procedure: See Appendix I

Results: See Tables 1 through 4 and Appendix II

Conclusion: Subject to reexamination in the light of later findings, the following is concluded:

"The administration of up to 900 mg/kg (body weight) of the test material to pregnant rats for 10 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls."

Comment: Attention is called to the fact that this is the ninth of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 36 compounds will have been tested in 18 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of control values will greatly enhance the statistical value of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge

Kenneth Morgareidge, Ph.D.
Vice President

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 81 through 86

Material: FDA 71-16

Table 1

Fate Summary
(Rats)

Date July 17, 1972

Laboratory No. 0894 f

Group	Material	Dose ** mg/kg	Total		At Term	
			Mated	Pregnant	Surviving (Total)	Number Pregnant
81	Sham	0.0	24	23	24	23
82	Aspirin*	250.0	24	22	24	22
83	FDA 71-16	9.0	24	23	24	23
84	FDA 71-16	42.0	24	24	24	24
85	FDA 71-16	200.0	24	24	24	24
86	FDA 71-16	900.0	24	20	23	20

* Positive Control
** Administered as a suspension in anhydrous corn oil; 1 ml per kg of body weight

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group: 81 through 86

Material: FDA 71-16

Date: July 17, 1972

Laboratory No.: 0894 f

Table 2
Reproduction Data
(Rats)

Group:	81	82	83	84	85	86
Dose (mg/kg):	Sham	Aspirin**	9.0	42.0	200.0	900.0
Pregnancies						
Total No.	23	22	23	24	24	20
Died or Aborted (before Day 20)	0	0	0	0	0	1
To term (on Day 20)	23	22	23	24	24	20
Corpora Lutea						
Total No.	264	248	277	275	269	225
Average/dam mated	11.0	10.3	11.5	11.5	11.2	9.38
Live Litters						
Total No.*	22	8	23	23	24	20
Implant Sites						
Total No.	261	233	276	266	262	221
Average/dam*	11.3	10.6	12.0	11.1	10.9	11.1
Resorptions						
Total No.*	4	169	8	13	7	3
Dams with 1 or more sites resorbed	3	19	6	2	7	3
Dams with all sites resorbed	1	14	0	1	0	0
Per cent partial resorptions	13.0	86.4	26.1	8.33	29.2	15.0
Per cent complete resorptions	4.35	63.6	--	4.17	--	--
Live Fetuses						
Total No.	257	63	268	253	255	218
Average/dam*	11.2	2.86	11.7	10.5	10.6	10.9
Sex ratio (M/F)	0.85	1.06	0.90	0.98	0.90	0.70
Dead Fetuses						
Total No.*	0	1	0	0	0	0
Dams with 1 or more dead	--	1	--	--	--	--
Dams with all dead	--	--	--	--	--	--
Per cent partial dead	--	4.55	--	--	--	--
Per cent all dead						
Average Fetus Weight, g	3.45	1.95	3.53	3.53	3.63	3.46

*Includes only those dams examined at term.
**Positive Control: 250 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 | Laboratory No. 0894 f

Table 3

Material FDA 71-16 | Date July 17, 1972

Summary of Skeletal Findings (Rats)

Findings	Group No.	81	82	83	84	85	86
	Dose (mg/kg)	Sham	Aspirin**	9	42	200	900
Live Fetuses Examined (at term)		171/22	42/8	178/23	169/23	172/24	149/20
Sternebrae							
Incomplete oss.		22/10	40/8	21/9	29/17	26/17	29/13
Scrambled							
Bipartite				1/1			
Fused							
Extra		1/1					
Missing		2/2	34/8				
Other							
Ribs							
Incomplete oss.			12/5			2/2	
Fused/split			2/2				
Wavy		4/4	17/5	6/3	5/4	4/4	11/6
Less than 12			2/1				
More than 13			20/6				
Other							
Vertebrae							
Incomplete oss.		9/7	40/8	11/9	5/5	8/6	9/4
Scrambled							
Fused			1/1				
Extra ctrs. oss.							
Scoliosis			6/2				
Tail defects							
Other							
Skull							
Incomplete closure		23/9	29/8	17/7	20/11	6/5	19/9
Missing							
Craniostosis			6/1				
Other							
Extremities							
Incomplete oss.			13/4				
Missing							
Extra							
Miscellaneous							
Hyoid; missing		22/8	27/7	25/11	14/9	16/9	15/4
Hyoid; reduced		3/2	1/1	5/5	3/2	1/1	2/1

* Numerator=Number of fetuses affected; Denominator=Number of litters affected
** Positive control at 250 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 Date July 17, 1972

Material FDA 71-16 Laboratory No. 0894 f

Table 3-a

Summary of Soft Tissue Abnormalities

(Rats)

Group	Material*	Dose level mg/kg	Dam	Pup	Description
82	Aspirin	250.0	A 4243	3	Craniocoele
				2	Acrania
				1	Spina bifida
			A 4245	3	Acrania, craniocoele, spina bifida
			A 4264	1	Acrania, craniocoele, spina bifida

* Positive control

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86

Species Rats

Table 4

Average Body Weights*

Date July 17, 1972

Laboratory No. 0894 f

Group	Material	Dose Level	Day 0	6	11	15	20**
		mg/kg	g				
81	Sham	0.0	206	224	247	272	338 (23)
82	Aspirin***	250.0	203	222	235	252	272 (22)
83	FDA 71-16	9.0	206	227	249	278	342 (23)
84	FDA 71-16	42.0	204	224	247	268	331 (24)
85	FDA 71-16	200.0	200	219	240	264	331 (24)
86	FDA 71-16	900.0	201	222	236	257	322 (20)

* Of pregnant dams
** Number of surviving dams in parentheses (c.f. Table 1)
*** Positive control

Appendix I

Teratology Study in Rats

Virgin adult female albino rats (Wistar derived stock) were individually housed in mesh bottom cages in temperature and humidity-controlled quarters with free access to food and fresh tap water. They were mated with young adult males, and observation of the vaginal sperm plug was considered Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 15 of gestation, the females were dosed with the indicated dosages by oral intubation; the controls were sham treated.

Body weights were recorded on Days 0, 6, 11, 15, and 20 of gestation. All animals were observed daily for appearance and behavior with particular attention to food consumption and weight, in order to rule out any abnormalities which may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 20 all dams were subjected to Caesarean section under surgical anesthesia, and the numbers of implantation sites, resorption sites, and live and dead fetuses were recorded. The body weights of the live pups were also recorded. The urogenital tract of each dam was examined in detail for anatomical normality.

All fetuses were examined grossly for the presence of external congenital abnormalities. One-third of the fetuses of each litter underwent detailed visceral examinations employing 10X magnification. The remaining two-thirds were cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 81 | Appendix II | Date July 17, 1972

Material Sham | Reproduction Data in Rats (Individual) | Laboratory No. 0894

Dose 0.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
S 4241	P	11	11	11		4	7		3.71	
S 4242	P	14	14	14		6	8		3.40	
S 4243	P	10	10	10		4	6		3.92	
S 4244	P	11	11	11		3	8		3.22	
S 4245	P	10	10	10		3	7		3.46	
S 4246	NP	0	0						----	
S 4247	P	14	12	11		8	3	1	3.45	
S 4248	P	11	11	11		6	5		3.35	
S 4249	P	14	14	14		7	7		3.90	
S 4250	P	12	12	12		4	8		3.46	
S 4251	P	12	12	12		2	10		3.29	
S 4252	P	12	12	11		3	8	1	3.36	
S 4253	P	12	11	11		7	4		3.78	
S 4254	P	13	13	13		7	6		3.72	
S 4255	P	12	12	12		7	5		2.98	
S 4256	P	12	12	12		7	5		3.38	
S 4257	P	12	12	12		6	6		3.38	
S 4258	P	12	12	12		6	6		3.21	
S 4259	P	12	12	12		8	4		3.38	
S 4260	P	12	12	12		4	8		3.34	
S 4261	P	11	11	11		5	6		3.40	
S 4262	P	13	13	13		7	6		3.15	
S 4263	P	2	2					2	----	
S 4264	P	10	10	10		4	6		3.72	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 82

Appendix II

Date July 17, 1972

Material Aspirin

Reproduction Data in Rats (Individual)

Laboratory No. 0894

Dose 250.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
A 4241	P	8	3					3	----	
A 4242	P	11	11	11		7	4		2.77	
A 4243	P	13	13	13		6	7		2.06	
A 4244	P	15	14	9	1	4	6	4	1.82	
A 4245	P	12	12	6		2	4	6	1.45	
A 4246	P	13	13	1		0	1	12	2.10	
A 4247	P	12	12					12	----	
A 4248	NP	10	0						----	
A 4249	P	12	12					12	----	
A 4250	P	10	9					9	----	
A 4251	P	12	12					12	----	
A 4252	P	11	5					5	----	
A 4253	P	12	12					12	----	
A 4254	P	11	11					11	----	
A 4255	P	9	9					9	----	
A 4256	P	11	10					10	----	
A 4257	NP	0	0						----	
A 4258	P	13	12					12	----	
A 4259	P	12	12					12	----	
A 4260	P	12	12					12	----	
A 4261	P	7	7					7	----	
A 4262	P	9	9	6		5	1	3	1.63	
A 4263	P	9	9	3		2	1	6	1.67	
A 4264	P	14	14	14		7	7		2.12	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 83 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Rats (Individual) | Laboratory No. 0894 f

Dose 9.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 4001	P	11	11	10		5	5	1	3.85	
F 4002	P	12	12	12		5	7		3.80	
F 4003	P	10	10	9		1	8	1	3.51	
F 4004	P	11	11	11		5	6		4.08	
F 4005	P	14	13	12		5	7	1	3.30	
F 4006	P	11	11	11		6	5		3.35	
F 4007	P	11	11	10		6	4	1	3.22	
F 4008	P	13	13	13		3	10		4.96	
F 4009	P	10	10	7		1	6	3	3.06	
F 4010	P	14	14	14		6	8		3.81	
F 4011	P	10	10	10		7	3		3.47	
F 4012	P	11	11	11		5	6		3.64	
F 4013	NP	0	0						----	
F 4014	P	10	10	10		5	5		3.35	
F 4015	P	15	15	15		7	8		3.53	
F 4016	P	15	15	15		11	4		3.49	
F 4017	P	11	11	10		7	3	1	3.41	
F 4018	P	10	10	10		4	6		3.33	
F 4019	P	14	14	14		5	9		3.09	
F 4020	P	15	15	15		4	11		3.27	
F 4021	P	14	14	14		10	4		3.18	
F 4022	P	10	10	10		8	2		3.62	
F 4023	P	13	13	13		4	9		3.32	
F 4024	P	12	12	12		7	5		3.49	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEAR LABORATORIES, INC.

Group 84 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Rats (Individual) | Laboratory No. 0894 f

Dose 42.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 4031	P	12	12	12		6	6		3.89	
F 4032	P	11	9	9		4	5		3.71	
F 4033	P	11	10	10		5	5		3.78	
F 4034	P	9	7	7		2	5		3.76	
F 4035	P	11	11	11		6	5		3.67	
F 4036	P	11	11	11		3	8		4.00	
F 4037	P	10	10	10		6	4		3.75	
F 4038	P	10	10	10		4	6		3.48	
F 4039	P	11	11	11		5	6		3.19	
F 4040	P	12	12	12		8	4		3.68	
F 4041	P	10	9	9		6	3		3.56	
F 4042	P	13	13	13		8	5		3.36	
F 4043	P	15	15	15		7	8		2.67	
F 4044	P	14	14	14		9	5		3.57	
F 4045	P	13	13	13		9	4		3.86	
F 4046	P	12	12					12	----	
F 4047	P	10	9	9		7	2		3.64	
F 4048	P	12	10	10		3	7		3.64	
F 4049	P	12	12	12		4	8		2.96	
F 4050	P	10	10	10		5	5		3.40	
F 4051	P	10	10	10		4	6		3.37	
F 4052	P	12	12	12		5	7		3.53	
F 4053	P	12	12	11		3	8	1	3.38	
F 4054	P	12	12	12		6	6		3.34	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 85 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Rats (Individual) | Laboratory No. 0894 f

Dose 200.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 4061	P	10	10	10		4	6		3.81	
F 4062	P	12	12	12		9	3		3.82	
F 4063	P	6	6	6		2	4		4.05	
F 4064	P	7	4	4		2	2		5.35	
F 4065	P	11	11	11		5	6		3.80	
F 4066	P	11	11	11		5	6		3.98	
F 4067	P	11	11	11		5	6		3.73	
F 4068	P	9	9	8		3	5	1	3.64	
F 4069	P	13	13	13		7	6		3.30	
F 4070	P	9	9	8		4	4	1	3.75	
F 4071	P	15	12	11		6	5	1	3.18	
F 4072	P	13	13	13		6	7		3.35	
F 4073	P	10	10	9		3	6	1	3.69	
F 4074	P	10	10	10		6	4		3.93	
F 4075	P	13	10	10		8	2		3.65	
F 4076	P	13	13	13		7	6		3.61	
F 4077	P	13	13	13		6	7		3.75	
F 4078	P	12	12	12		6	6		3.33	
F 4079	P	12	13	12		4	8	1	2.60	
F 4080	P	13	13	12		3	9	1	2.86	
F 4081	P	9	9	9		4	5		3.39	
F 4082	P	14	14	14		7	7		3.38	
F 4083	P	9	10	9		5	4	1	3.67	
F 4084	P	14	14	14		4	10		3.51	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEAR LABORATORIES, INC.

Group 86

Appendix II

Date July 17, 1972

Material FDA 71-16

Reproduction Data in Rats (Individual)

Laboratory No. 0894 f

Dose 900.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 4091	P	9	9	9		3	6		3.86	
F 4092	P	10	10	10		5	5		3.72	
F 4093	P	13	13	13		8	5		2.86	
F 4094	P	12	12	12		3	9		2.83	
F 4095	NP	0	0						----	Died Day 16
F 4096	NP	6	0						----	
F 4097	NP	7	0						----	
F 4098	NP	10	0						----	
F 4099	P	13	13	13		8	5		3.38	
F 4100	P	9	9	9		5	4		3.49	
F 4101	P	12	11	11		3	8		3.50	
F 4102	P	10	10	10		4	6		3.42	
F 4103	P	10	10	10		4	6		3.62	
F 4104	P	14	13	13		5	8		3.52	
F 4105	P	11	11	11		6	5		3.36	
F 4106	P	14	14	13		4	9	1	3.57	
F 4107	P	10	10	10		5	5		3.69	
F 4108	P	13	13	13		6	7		3.56	
F 4109	P	11	11	10		2	8	1	3.35	
F 4110	P	12	10	10		4	6		3.76	
F 4111	P	10	10	10		3	7		3.68	
F 4112	P	9	9	9		4	5		3.48	
F 4113	P	10	10	9		3	6	1	3.26	
F 4114	P	13	13	13		5	8		3.31	

* P = Pregnant; NP = Not Pregnant

HAMSTERS

Food and Drug Research Laboratories
INCORPORATED

Maurice Avenue at 58th Street
Maspeth, New York 11378
Telephone: TWining 4-0800
Cable: Foodlabs, New York

FINAL REPORT

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date August 25, 1972

Laboratory No. 0895 f
Contract No. FDA 71-260

Sample: Fine tan powdered material

Marking: FDA 71-16 (Guar Gum)

Examination Requested: Teratologic evaluation of FDA 71-16 in hamsters

Procedure: See Appendix I

Results: See Tables 1 through 4 and Appendix II

Conclusion: Subject to reexamination in the light of later findings, the following is concluded:

"The administration of up to 600 mg/kg (body weight) of the test material to pregnant hamsters for 5 consecutive days had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls."

Comment: Attention is called to the fact that this is the ninth of a series of reports which will be issued in accordance with the terms of the contract cited above. Eventually, a total of at least 36 compounds will have been tested in 18 pairs; each pair being run concurrently against one sham-treated control and one positive control group. Because of the inherent variability of biological data of the type dealt with here, the accumulation and pooling of sequential sets of control values will greatly enhance the statistical value of the findings and the ultimate reliability of the test results.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge

Kenneth Morgareidge, Ph.D
Vice President

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: 81 through 86

Material: FDA 71-16

Table 1

Fate Summary
(Hamsters)

Date July 17, 1972

Laboratory No. 0895 f

Group	Material	Dose** mg/kg	Total		At Term	
			Mated	Pregnant	Surviving (Total)	Number Pregnant
81	Sham	0	21	21	19	19
82	Aspirin*	250	23	21	23	21
83	FDA 71-16	6	22	21	22	21
84	FDA 71-16	28	22	20	22	20
85	FDA 71-16	130	22	21	22	21
86	FDA 71-16	600	20	20	20	20

* Positive Control

** Administered as a suspension in anhydrous corn oil; 1 ml per kg of body weight

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group: 81 through 86

Material: FDA 71-16

Date: July 17, 1972

Laboratory No.: 0895 f

Table 2
Reproduction Data
(Hamsters)

Group:	81	82	83	84	85	86
Dose (mg/kg):	Sham	Aspirin**	6	28	130	600
Pregnancies						
Total No.	21	21	21	20	21	20
Died or Aborted (before Day 14)	2	0	0	0	0	0
To term (on Day 14)	19	21	21	20	21	20
Corpora Lutea						
Total No.						
Average/dam mated						
Live Litters						
Total No.*	19	21	21	20	21	20
Implant Sites						
Total No.	231	262	259	250	253	256
Average/dam*	12.2	12.5	12.3	12.5	12.0	12.8
Resorptions						
Total No.*	10	9	6	9	10	8
Dams with 1 or more sites resorbed	5	7	4	5	6	6
Dams with all sites resorbed	0	0	0	0	0	0
Per cent partial resorptions	26.3	33.3	19.0	25.0	28.6	30.0
Per cent complete resorptions	-	-	-	-	-	-
Live Fetuses						
Total No.	219	253	253	240	243	248
Average/dam*	11.5	12.0	12.0	12.0	11.6	12.4
Sex ratio (M/F)	0.44	0.68	0.54	0.48	0.52	0.39
Dead Fetuses						
Total No.*	2	0	0	1	0	0
Dams with 1 or more dead	2	-	-	1	-	-
Dams with all dead	0	-	-	-	-	-
Per cent partial dead	10.5	-	-	5.00	-	-
Per cent all dead	-	-	-	-	-	-
Average Fetus Weight, g	1.78	1.80	1.74	1.80	1.78	1.75

*Includes only those dams examined at term.
**Positive Control: 250 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 | Laboratory No. 0895 f

Table 3

Material FDA 71-16 | Date July 17, 1972

Summary of Skeletal Findings
(Hamsters)

Findings	Group No.	81	82	83	84	85	86
	Dose (mg/kg)	Sham	Aspirin**	6	28	130	600
Live Fetuses Examined (at term)		154/19	177/21	169/21	167/20	167/21	174/20
Sternebrae							
Incomplete oss.		48/16	52/18	84/19	79/20	54/17	78/20
Scrambled							
Bipartite		25/11	23/13	25/16	18/10	9/8	17/11
Fused							
Extra							
Missing		17/8	39/15	33/13	13/9	32/11	24/9
Other							
Ribs							
Incomplete oss.							
Fused/split							
Wavy							
Less than 12							
More than 13		13/8	25/8	26/15	45/18	14/8	35/16
Other							
Vertebrae							
Incomplete oss.							1/1
Scrambled							
Fused							
Extra ctrs. oss.							
Scoliosis							
Tail defects			1				
Other							
Skull							
Incomplete closure							
Missing							
Craniostosis							
Other							
Extremities							
Incomplete oss.						13/4	
Missing							
Extra							
Miscellaneous							
Hyoid; missing		2/2	7/4			5/3	
Hyoid; reduced		3/2	14/9			19/11	

* Numerator=Number of fetuses affected; Denominator=Number of litters affected
** Positive control 250 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86 Date July 17, 1972

Material FDA 71-16 Laboratory No. 0895 f

Table 3-a

Summary of Soft Tissue Abnormalities

(Hamsters)

Group	Material	Dose level mg/kg	Dam	Number of Pups	Description

None Observed

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups 81 through 86

Species Hamsters

Table 4

Average Body Weights*

Date July 17, 1972

Laboratory No. 0895

Group	Material	Dose Level	Day 0	6	8	10	15**
		mg/kg	g				
81	Sham	0.0	98.7	103.8	101.9	113.7	135.3 (19)
82	Aspirin***	250.0	101.4	106.4	110.7	122.2	143.8 (21)
83	FDA 71-16	6.0	97.4	102.2	107.0	116.4	139.8 (21)
84	FDA 71-16	28.0	101.4	107.8	113.3	125.2	147.0 (20)
85	FDA 71-16	130.0	100.1	102.5	106.5	117.2	136.8 (21)
86	FDA 71-16	600.0	100.1	103.7	106.4	117.6	140.9 (20)

* Of pregnant dams
** Number of surviving dams in parentheses (c.f. Table 1)
*** Positive control:

Appendix I

Teratology Study in Hamsters

Virgin adult female golden hamsters from an outbred strain were individually housed in mesh bottom cages in temperature and humidity controlled quarters with free access to food and fresh tap water at all times. They were mated (1 to 1) with mature males and the appearance of motile sperm in the vaginal smear was considered as Day 0 of gestation. Beginning on Day 6 and continuing daily through Day 10 of gestation, the indicated dose levels of the test material were administered by oral intubation; the controls were sham-treated.

Body weights were recorded on Days 0, 8, 10, and 14 of the gestation period. All animals were observed daily for appearance and behavior with particular attention to food consumption in order to better recognize any abnormalities resulting from anorexic effects in the pregnant animal.

On Day 14, all animals were subjected to Caesarian section under deep anesthesia and the numbers of implantation sites, resorption sites, live and dead fetuses were recorded. All live pups were weighed and the genital tract of each dam was examined for any anatomical abnormalities.

All fetuses were examined grossly for the presence of external congenital defects and one-third of each litter underwent detailed visceral examination under 10X magnification. The remaining two-thirds of the pups were cleared in potassium hydroxide, stained with alizarin red dye, and examined for the presence of sketal abnormalities.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 81 | Appendix II | Date July 17, 1972

Material Sham | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895

Dose 0.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
S 5241	P		12	12		--	--		----	Died Day 11
S 5242	P		11	11		2	9		1.81	
S 5243	P		15	15		4	11		1.75	
S 5244	P		14	10		2	8	4	1.73	
S 5245	P		14	14		4	10		1.64	
S 5246	P		12	12		--	--		----	Died Day 13
S 5247	P		10	10		2	8		1.85	
S 5248	P		11	11		6	5		1.91	
S 5249	P		13	13		6	7		1.73	
S 5250	P		14	14		3	11		1.98	
S 5251	P		10	9		3	6	1	1.85	
S 5252	P		11	9	1	2	7	1	1.93	
S 5253	P		11	11		1	10		2.08	
S 5254	P		12	12		0	12		1.65	
S 5255	P		13	10		1	9	3	1.67	
S 5256	P		12	11	1	2	9		1.48	
S 5257	P		11	11		7	4		2.05	
S 5258	P		14	14		8	6		1.74	
S 5259	P		12	12		6	6		1.67	
S 5260	P		11	11		5	6		1.75	
S 5261	P		12	11		3	8	1	1.62	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 82 | Appendix II | Date July 17, 1972

Material Aspirin | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895

Dose 250.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
A 5241	P		12	11		1	10	1	1.81	
A 5242	P		10	8		1	7	2	1.84	
A 5243	P		13	13		4	9		1.92	
A 5244	P		13	13		8	5		1.91	
A 5245	P		10	8		4	4	2	1.86	
A 5246	P		12	12		6	6		1.75	
A 5247	P		14	14		5	9		1.84	
A 5248	P		12	12		5	7		1.93	
A 5249	P		15	15		6	9		1.96	
A 5250	NP		0						----	
A 5251	P		12	11		7	4	1	1.75	
A 5252	P		11	11		4	7		1.86	
A 5253	NP		0						----	
A 5254	P		11	11		5	6		1.52	
A 5255	P		9	8		1	7	1	1.90	
A 5256	P		16	16		5	11		1.70	
A 5257	P		17	17		9	8		1.76	
A 5258	P		14	14		4	10		1.79	
A 5259	P		15	15		10	5		1.64	
A 5260	P		11	10		5	5	1	2.02	
A 5261	P		11	11		4	7		1.74	
A 5262	P		13	12		5	7	1	1.58	
A 5263	P		11	11		3	8		1.78	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 83 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895 f

Dose 6.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 5001	P		12	12		2	10		1.82	
F 5002	P		13	13		3	9		1.68	
F 5003	P		13	11		3	8	2	1.65	
F 5004	P		11	11		3	8		2.01	
F 5005	P		12	11		6	5	1	1.76	
F 5006	P		13	13		5	8		1.87	
F 5007	NP		0						----	
F 5008	P		12	12		6	6		1.79	
F 5009	P		15	15		9	6		1.72	
F 5010	P		8	8		2	6		2.41	
F 5011	P		11	9		3	6	2	1.57	
F 5012	P		10	9		--	--	1	1.93	
F 5013	P		15	15		4	11		1.68	
F 5014	P		11	11		2	9		1.80	
F 5015	P		13	13		3	10		1.73	
F 5016	P		14	14		1	13		1.67	
F 5017	P		12	12		6	6		1.52	
F 5018	P		16	16		7	9		1.70	
F 5019	P		9	9		--	--		1.86	
F 5020	P		13	13		5	8		1.63	
F 5021	P		13	13		4	9		1.59	
F 5022	P		13	13		5	8		1.62	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 84 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895 f

Dose 28.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 5031	NP		0						----	
F 5032	P		14	14		5	9		1.73	
F 5033	NP		0						----	
F 5034	P		5	3		2	1	2	2.16	
F 5035	P		14	14		8	6		1.82	
F 5036	P		13	13		7	6		1.79	
F 5037	P		10	10		3	7		1.95	
F 5038	P		12	12		4	8		1.93	
F 5039	P		11	11		3	8		1.61	
F 5040	P		14	13		4	9	1	1.91	
F 5041	P		13	11		5	6	2	1.68	
F 5042	P		10	10		3	7		1.77	
F 5043	P		12	12		3	9		1,93	
F 5044	P		12	12		0	12		1.89	
F 5045	P		14	14		1	13		1.84	
F 5046	P		16	14		5	9	2	1.77	
F 5047	P		16	16		4	12		1.96	
F 5048	P		12	12		5	7		1.66	
F 5049	P		15	15		7	8		1.79	
F 5050	P		13	12	1	5	7		1.73	
F 5051	P		11	9		1	8	2	1.66	
F 5052	P		13	13		3	10		1.82	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 85 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895 f

Dose 130.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 5061	P		11	11		2	9		1.54	
F 5062	P		12	8		3	5	4	1.55	
F 5063	P		11	11		4	7		1.88	
F 5064	P		12	10		7	3	2	1.81	
F 5065	NP		0						----	
F 5066	P		13	13		6	7		1.85	
F 5067	P		11	11		4	7		2.01	
F 5068	P		10	10		5	5		1.90	
F 5069	P		12	11		5	6	1	1.65	
F 5070	P		12	11		0	11	1	1.60	
F 5071	P		13	13		2	11		1.97	
F 5072	P		11	10		4	6	1	1.83	
F 5073	P		13	13		2	11		1.87	
F 5074	P		7	7		2	5		1.95	
F 5075	P		12	12		5	7		1.88	
F 5076	P		14	14		8	6		1.72	
F 5077	P		11	11		7	4		1.62	
F 5078	P		14	14		2	12		1.80	
F 5079	P		16	16		4	12		1.82	
F 5080	P		10	10		3	7		1.84	
F 5081	P		14	14		5	9		1.84	
F 5082	P		14	13		4	9	1	1.55	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group 86 | Appendix II | Date July 17, 1972

Material FDA 71-16 | Reproduction Data in Hamsters (Individual) | Laboratory No. 0895 f

Dose 600.0 mg/kg

Dam No.	Fate*	Corpora Lutea	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
				Alive	Dead	M	F			
F 5091	P		12	12		0	12		1.98	
F 5092	P		14	12		4	8	2	1.92	
F 5093	P		12	11		--	--	1	1.47	
F 5094	P		14	14		5	9		1.81	
F 5095	P		14	14		8	6		1.80	
F 5096	P		15	15		5	10		2.02	
F 5097	P		14	14		6	8		1.83	
F 5098	P		15	15		8	7		1.99	
F 5099	P		14	14		6	8		1.62	
F 5100	P		10	9		1	8	1	1.91	
F 5101	P		11	9		0	9	2	1.73	
F 5102	P		12	12		1	4		1.43	
F 5103	P		15	15		3	12		1.85	
F 5104	P		11	11		2	9		1.57	
F 5105	P		14	14		3	11		1.64	
F 5106	P		12	11		2	9	1	1.49	
F 5107	P		14	14		6	8		1.64	
F 5108	P		12	12		4	8		1.90	
F 5109	P		11	11		5	6		1.56	
F 5110	P		10	9		1	8	1	1.76	

* P = Pregnant; NP = Not Pregnant

RABBITS

Food and Drug Research Laboratories
INCORPORATED

Maurice Avenue at 58th Street
Maspeth, New York 11378
Telephone: TWining 4-0800
Cable: Foodlabs, New York

FINAL REPORT

Submitted to: DHEW/Public Health Service
Food and Drug Administration CA-272
5600 Fishers Lane-Room 5C-13
Rockville, Maryland 20852

Date August 25, 1972

Laboratory No. 0896 f
Contract No. FDA 71-260

Sample: Fine tan powdered material

Marking: FDA 71-16 (Guar Gum)

Examination Requested: Teratologic evaluation of FDA 71-16 in rabbits

Procedure: (See Appendix I)

Results: (To Follow)

Conclusion:

(This test has been deferred due to unavailability of suitable rabbits.)

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Kenneth Morgareidge

Kenneth Morgareidge, Ph.D.
Vice President

Appendix I

Teratology Study in Rabbits

Virgin, adult, Dutch-belted female rabbits were individually housed in mesh bottom cages in temperature and humidity-controlled quarters with free access to food and fresh tap water. On Day 0, each doe was given an injection of 0.4 ml of human chorionic gonadotropin (400 IU) via the marginal ear vein. Three hours later, each doe was inseminated artificially with 0.3 ml of diluted semen from a proven donor buck using approximately 20×10^6 motile sperm according to the procedure described by Vogin et al (Pharmacologist 11, 282 (1969)). Beginning on Day 6 and continuing daily through Day 18 the females were dosed with the indicated dosages by oral intubation; the controls were sham treated.

Body weights were recorded on Days 0, 6, 12, 18, and 29 of gestation. All animals were observed daily for appearance and behavior, with particular attention to food consumption and body weight in order to rule out any abnormalities which may have occurred as a result of anorexic effects in the pregnant female animal.

On Day 29 all does were subjected to Caesarean section under surgical anesthesia, and the numbers of corpora lutea, implantation sites, resorption sites and live and dead fetuses were recorded. Body weights of the live pups were also recorded. The urogenital tract of each animal was examined in detail for normality. In addition alI fetuses underwent a detailed gross examination for the presence of external congenital abnormalities. The live fetuses of

each litter were then placed in an incubator for 24 hours for the evaluation of neonatal survival. All surviving pups were sacrificed, and all pups examined for visceral abnormalities (by dissection). All fetuses were then cleared in potassium hydroxide (KOH), stained with alizarin red S dye and examined for skeletal defects.